DESCRIPTION. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and theuse of the first person. This description is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential inforamtion. DO NOT EXCEED THE SPACE PROVIDED.

While autologous stem cell transplantation can provide curative therapy for up to 65% of germ cell tumors patients relapsing after initial therapy, those patients who relapse within 3 months of initial therapy, undergo multiple salvage regimens, or are refractory to induction therapy have only a 15% long-term survival. Recently, we noted that maintenance chemotherapy administered after transplantation appears to improve survival but was difficult to administer in most patients due to the significant sensitivity of post-transplantation marrow to chemotherapeutic agents. We hypothesize that introduction of the multiple drug resistance gene (MDR-1) into peripheral blood stem cells administered during transplantation may decrease hematotoxicity of post-transplantation chemotherapy and ultimately improve survival for refractory germ cell tumor patients. The proposed study is a pilot study to determine the feasibility of such an approach with the following specific aims:

1. Determine if transplantation of CD34+ PBSC exposed to the MDR-1 retroviral vector in the presence of recombinant fibronectin fragment will lead to engraftment of vector containing cells.
2. Determine if post-transplantation chemotherapy will provide a selective advantage for MDR-1 expressing bone marrow cells.
3. Evaluate the safety of retroviral mediated gene transfer using this transduction procedure.

There are three novel aspects of this proposal which are of scientific interest. First, unlike similar studies in breast cancer and ovarian cancer, we have demonstrated a clinical benefit to post-transplantation chemotherapy for germ cell tumors. Secondly, this protocol will utilize a novel recombinant fibronectin fragment which greatly increase gene transfer rates without requiring co-cultivation on stroma. Finally, the sequential administration of chemotherapy post-transplantation also provides an ideal setting to evaluate whether MDR-1 expressing cells are protected from *in vivo* chemotherapy administration.